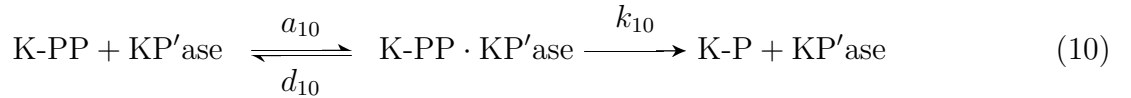
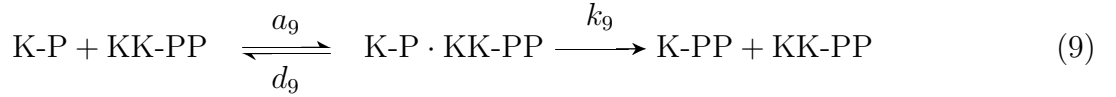
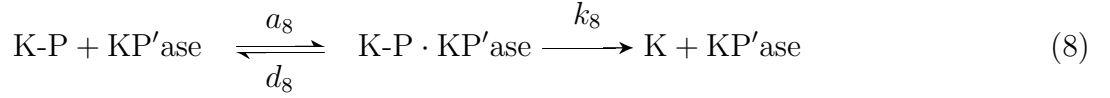
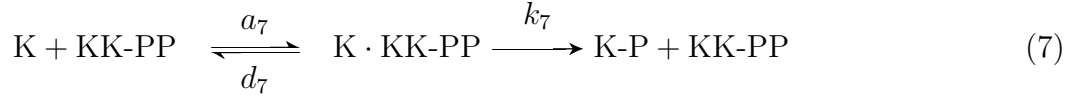
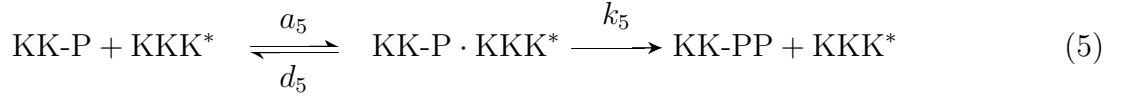
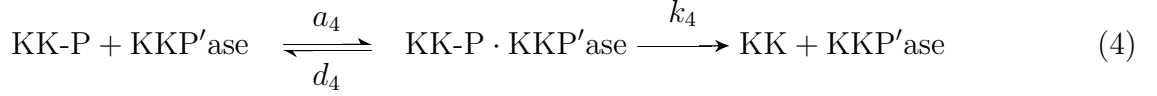
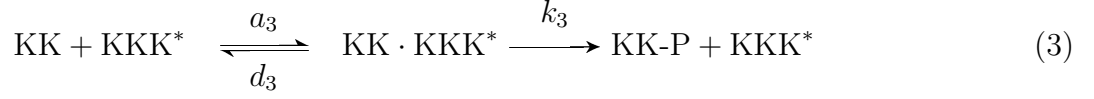
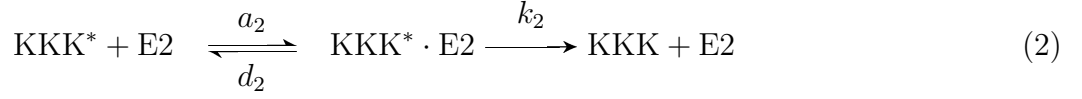
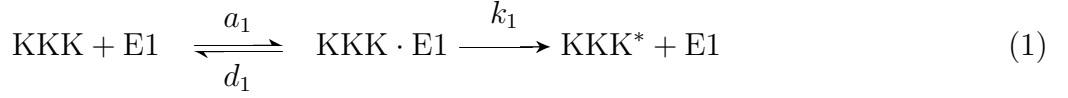


## Text S1

The Huang-Ferrell model is based on the following enzymatic reactions [26]:



We model the cascade using the following DAE system consisting of 15 ODEs and 7 algebraic equations.

$$\frac{d}{dt}[\text{KKK} \cdot \text{E1}] = a_1[\text{KKK}][\text{E1}] - (d_1 + k_1)[\text{KKK} \cdot \text{E1}] \quad (11)$$

$$\begin{aligned} \frac{d}{dt}[\text{KKK}^*] &= k_1[\text{KKK} \cdot \text{E1}] - a_2[\text{KKK}^*][\text{E2}] + d_2[\text{KKK}^* \cdot \text{E2}] \\ &\quad - a_3[\text{KKK}^*][\text{KK}] + (k_3 + d_3)[\text{KK} \cdot \text{KKK}^*] \\ &\quad - a_5[\text{KK-P}][\text{KKK}^*] + (k_5 + d_5)[\text{KK-P} \cdot \text{KKK}^*] \end{aligned} \quad (12)$$

$$\frac{d}{dt}[\text{KKK}^* \cdot \text{E2}] = a_2[\text{KKK}^*][\text{E2}] - (d_2 + k_2)[\text{KKK}^* \cdot \text{E2}] \quad (13)$$

$$\frac{d}{dt}[\text{KK} \cdot \text{KKK}^*] = a_3[\text{KK}][\text{KKK}^*] - (d_3 + k_3)[\text{KK} \cdot \text{KKK}^*] \quad (14)$$

$$\begin{aligned}\frac{d}{dt}[\text{KK-P}] &= k_3[\text{KK} \cdot \text{KKK}^*] - a_4[\text{KK-P}][\text{KKP}'\text{ase}] \\ &\quad + d_4[\text{KK-P} \cdot \text{KKP}'\text{ase}] - a_5[\text{KK-P}][\text{KKK}^*] \\ &\quad + d_5[\text{KK-P} \cdot \text{KKK}^*] + k_6[\text{KK-PP} \cdot \text{KKP}'\text{ase}]\end{aligned}\quad (15)$$

$$\frac{d}{dt}[\text{KK-P} \cdot \text{KKP}'\text{ase}] = a_4[\text{KK-P}][\text{KKP}'\text{ase}] - (d_4 + k_4)[\text{KK-P} \cdot \text{KKP}'\text{ase}] \quad (16)$$

$$\frac{d}{dt}[\text{KK-P} \cdot \text{KKK}^*] = a_5[\text{KK-P}][\text{KKK}^*] - (d_5 + k_5)[\text{KK-P} \cdot \text{KKK}^*] \quad (17)$$

$$\begin{aligned}\frac{d}{dt}[\text{KK-PP}] &= k_5[\text{KK-P} \cdot \text{KKK}^*] - a_6[\text{KK-PP}][\text{KKP}'\text{ase}] \\ &\quad + d_6[\text{KK-PP} \cdot \text{KKP}'\text{ase}] - a_7[\text{KK-PP}][\text{K}] \\ &\quad + (d_7 + k_7)[\text{K} \cdot \text{KK-PP}] - a_9[\text{K-P}][\text{KK-PP}] \\ &\quad + (d_9 + k_9)[\text{K-P} \cdot \text{KK-PP}]\end{aligned}\quad (18)$$

$$\begin{aligned}\frac{d}{dt}[\text{KK-PP} \cdot \text{KKP}'\text{ase}] &= a_6[\text{KK-PP}][\text{KKP}'\text{ase}] \\ &\quad - (d_6 + k_6)[\text{KK-PP} \cdot \text{KKP}'\text{ase}]\end{aligned}\quad (19)$$

$$\frac{d}{dt}[\text{K} \cdot \text{KK-PP}] = a_7[\text{K}][\text{KK-PP}] - (d_7 + k_7)[\text{K} \cdot \text{KK-PP}] \quad (20)$$

$$\begin{aligned}\frac{d}{dt}[\text{K-P}] &= k_7[\text{K} \cdot \text{KK-PP}] - a_8[\text{K-P}][\text{KP}'\text{ase}] \\ &\quad + d_8[\text{K-P} \cdot \text{KP}'\text{ase}] - a_9[\text{K-P}][\text{KK-PP}] \\ &\quad + d_9[\text{K-P} \cdot \text{KK-PP}] + k_{10}[\text{K-PP} \cdot \text{KP}'\text{ase}]\end{aligned}\quad (21)$$

$$\frac{d}{dt}[\text{K-P} \cdot \text{KP}'\text{ase}] = a_8[\text{K-P}][\text{KP}'\text{ase}] - (d_8 + k_8)[\text{K-P} \cdot \text{KP}'\text{ase}] \quad (22)$$

$$\frac{d}{dt}[\text{K-P} \cdot \text{KK-PP}] = a_9[\text{K-P}][\text{KK-PP}] - (d_9 + k_9)[\text{K-P} \cdot \text{KK-PP}] \quad (23)$$

$$\begin{aligned}\frac{d}{dt}[\text{K-PP}] &= k_9[\text{K-P} \cdot \text{KK-PP}] - a_{10}[\text{K-PP}][\text{KP}'\text{ase}] \\ &\quad + d_{10}[\text{K-PP} \cdot \text{KP}'\text{ase}]\end{aligned}\quad (24)$$

$$\frac{d}{dt}[\text{K-PP} \cdot \text{KP}'\text{ase}] = a_{10}[\text{K-PP}][\text{KP}'\text{ase}] - (d_{10} + k_{10})[\text{K-PP} \cdot \text{KP}'\text{ase}] \quad (25)$$

$$\begin{aligned}0 &= [\text{KKK}] + [\text{KKK}^*] + [\text{KKK} \cdot \text{E1}] + [\text{KKK}^* \cdot \text{E2}] \\ &\quad + [\text{KK} \cdot \text{KKK}^*] + [\text{KK-P} \cdot \text{KKK}^*] - \text{KKK}_{\text{tot}}\end{aligned}\quad (26)$$

$$\begin{aligned}0 &= [\text{KK}] + [\text{KK-P}] + [\text{KK-PP}] + [\text{KK} \cdot \text{KKK}^*] \\ &\quad + [\text{KK-P} \cdot \text{KKK}^*] + [\text{KK-P} \cdot \text{KKP}'\text{ase}] \\ &\quad + [\text{KK-PP} \cdot \text{KKP}'\text{ase}] + [\text{K} \cdot \text{KK-PP}] \\ &\quad + [\text{K-P} \cdot \text{KK-PP}] - \text{KK}_{\text{tot}}\end{aligned}\quad (27)$$

$$\begin{aligned}0 &= [\text{K}] + [\text{K-P}] + [\text{K-PP}] + [\text{K} \cdot \text{KK-PP}] \\ &\quad + [\text{K-P} \cdot \text{KK-PP}] + [\text{K-P} \cdot \text{KP}'\text{ase}] \\ &\quad + [\text{K-PP} \cdot \text{KP}'\text{ase}] - \text{K}_{\text{tot}}\end{aligned}\quad (28)$$

$$0 = [\text{E1}] + [\text{KKK} \cdot \text{E1}] - \text{E1}_{\text{tot}} \quad (29)$$

$$0 = [\text{E2}] + [\text{KKK}^* \cdot \text{E2}] - \text{E2}_{\text{tot}} \quad (30)$$

$$0 = [\text{KKP}'_{\text{ase}}] + [\text{KK-P} \cdot \text{KKP}'_{\text{ase}}] + [\text{KK-PP} \cdot \text{KKP}'_{\text{ase}}] - \text{KKP}'_{\text{ase}_{\text{tot}}} \quad (31)$$

$$0 = [\text{KP}'_{\text{ase}}] + [\text{K-P} \cdot \text{KP}'_{\text{ase}}] + [\text{K-PP} \cdot \text{KP}'_{\text{ase}}] - \text{KP}'_{\text{ase}_{\text{tot}}} \quad (32)$$